Stem Cell-Based Immunomodulation After Stroke: Effects on Brain Repair Processes.

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Public Summary:
Stroke is a major cause of death and disability world-wide. The inflammatory response is crucial to the physiological processes of ischemic stroke. It begins in the vascular system directly after a stroke event, continues in the brain, and systemically throughout all disease stages. Immune system responses are tightly controlled, and have both helpful and harmful properties after stroke; inflammation can result in considerable brain damage and inhibition of brain repair, Changes in different inflammatory processes mean that the immune response is a strong determinant of brain restoration and patient survival after stroke. Directed changes to the immune response could therefore, be designed as a potential therapy to initiate stroke recovery. These types of changes can be achieved with stem cell (SC) therapy; it is now a widely investigated approach with multiple clinical trials for different diseases, including stroke (www.clinicaltrials.gov). Certain types of SCs are pluri- or multipotent and have the potential to create many neural cells, which may be important after stroke-based neuronal loss. Exogenous SC transplantations, primarily with neural stem/precursor cells (NSPCs) and mesenchymal-derived SCs (MSCs), have been examined using different delivery routes in various stroke animal models; increased functional recovery was often observed. Besides NSPCs and MSCs, mixed adult SC populations from bone marrow or umbilical cord blood have been examined, showing improved results as well. However, the time window in which these mixed cell populations can be effectively delivered seems to be narrower. This restricts their use to the acute and subacute stages after stroke as compared with the NSPCs and MSCs, which can be used in chronic stroke as well. Therefore, the focus of this Topical Review lies on NSPC and MSC therapy in stroke. Despite many studies, the exact mechanisms behind the brain restoring effects that are seen are not completely understood. It is thought that SC-based approaches can induce poststroke recovery via mechanisms such as: neuronal replacement, pro-motion of angiogenesis, induction of brain plasticity, reduction of cell death, or immunomodulation. This Topical Review is the first to link SC-induced immunomodulation to different proregenerative processes; understanding these interactions is essential to develop successful stroke therapies in the future.

Scientific Abstract: